Safety Data Sheet

N-Nitroso-N-methylurea

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, MUTAGENIC, AND TERATOGENIC. ALKALINE HYDROLYSIS PRODUCES DIAZOMETHANE, WHICH IS A HIGHLY TOXIC, IRRITATING, CARCINOGENIC, HIGHLY FLAMMABLE, AND EXPLOSIVE GAS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK MILK. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

N-Nitroso-N-methylurea (MNU) is toxic, carcinogenic, mutagenic, and teratogenic in animals and experimental test systems. Its primary use is for tumor induction and related research in experimental animals and as a research mutagen.

B. Chemical and Physical Data

1. Chemical Abstract No.: 684-93-5

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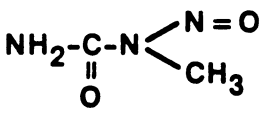
Synonyms:

MNU	NMH
NMU	1-Nitroso-1-methylurea
N-Methyl-N-nitrosourea (9CI)	N-Nitroso-N-methyl carbamide
Methylnitrosourea	N-Nitrosomethylurea
1-Methyl-1-nitrosourea	

Molecular formula: $C_2H_5N_3O_2$

structure: 

weight: 103.1

Density: No data.

Absorption spectroscopy: IR, UV, NMR spectra have been reported b Heyns and Roper (1974). UV (CH_2Cl_2): λ (log ϵ) = 231 (3.93), 393 (2.13), and 41 (2.08) (Mirvish, 1971).

Volatility: Nonvolatile. Air:water distribution coefficient is very low ($10^5 \cdot K < 0.2$ at 37°C) (Mirvish et al., 1976).

Solubility: 1.4% in water at room temperature. Soluble in polar organic solvents.

Description, appearance: Pale yellow crystals.

Boiling point: No data.

Melting point: 126°C (with decomposition) (Mirvish, 1971).

Stability: The pure compound is sensitive to humidity and light. It should be stored in the dark in tightly closed bottles at less than -10°C, and its purity should be checked periodically. Storage at room temperature has been known to result in explosion, probably due to the buildup of pressure (Sparrow, 1973). Stability in aqueous solutions is pH dependent, with maximum stability occurring at about pH 4 (Druckrey et al., 1967). It is hydrolyzed by alkali (liberating diazomethane, a highly toxic gas) and by strong acid.

Chemical reactivity: MNU is a strong alkylating agent and has been used as a source of diazomethane, which is released on alkali

12. Flash point: Does not apply.

13. Autoignition temperature: No data.

14. Flammable limits: Does not apply.

Fire, Explosion, and Reactivity Hazard Data

1. Dry chemical or carbon dioxide extinguishers may be used. Fire fighters should wear air-supplied respirators with full-face masks.

2. Decomposition products may be explosive. Sealed bottles at room temperature may explode due to gas pressure.

3. Sensitive to light and moisture.

4. Incompatible with water.

5. Alkaline hydrolysis produces diazomethane, which is a highly toxic, irritating, flammable, and explosive gas.

6. Avoid contact with alkaline solutions.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving MNU.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by MNU or the materials used for cleanup. If more than 1 g has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with a polar organic solvent, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing MNU shall be disposed of in sinks or general refuse. Surplus MNU or chemical waste streams contaminated with MNU shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing MNU shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing MNU shall

be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with MNU shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent material (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste dispo system. Radioactive waste containing MNU shall be handled i accordance with the NIH radioactive waste disposal system.

4. Storage: Store working quantities of MNU and its solutions in a safety refrigerator in the work area. Store stocks of MNU below -10°C in amber bottles with caps and Teflon cap liners. Do not store in ampoules since these could explode. Avoid exposure to light and moisture.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: MNU could be found in aerosols formed in the laboratory, but no reliable sampling method for this potenti hazard has been reported.

2. Separation and analysis: HPLC and TLC are appropriate for separation of nitrosamides. UV spectrophotometric detection has been used with HPLC (Heyns and Roper, 1974) and TLC (Mirvish and Chu, 1972) for detection and quantitative determination of nitrosoureas. MNU is also readily determined colorimetrically as nitrite after acidic hydrolysis (Preussmann and Schaper-Druckrey, 1972).

Biological Effects (Animal and Human)

1. Absorption: MNU is absorbed and produces toxic effects on application to skin of rodents and humans and by ingestion and parenteral injection.

2. Distribution: The label of intravenous or intragastric ^{14}C-MNU is rapidly and uniformly distributed to all body organs.

3. Metabolism and excretion: The high chemical and biological reactivity of MNU makes it unlikely that an enzymatic metabolism is involved in its action. Its breakdown leads to formation of methylcarbonium ions that alkylate proteins and nucleic acids (IARC, 1978). Excretion products have not been identified.

4. Toxic effects: Acute LD50s are 108, 110, and 180 mg/kg in rats (intravenous, intraperitoneal, and oral, respectively) and 144 mg/kg in mice (intraperitoneal). Two chief target organs are the eye (retinal atrophy, cataract) and the pancre

(diabetogenic effects, such as degeneration of islet cells, hyperglycemia). Other effects are depression of the hematopoietic system and degeneration of testes and ovaries. Some of these effects were observed after single doses of MNU. In humans, MNU has been used in clinical trials against lung tumors and Hodgkin's disease; nausea, vomiting, epigastric pain, and, to a lesser extent, diarrhea, leukopenia, and cutaneous rashes have been observed.

5. Carcinogenic effects: MNU is carcinogenic in all species so far tested. The effects are, in part, local and therefore vary with route of administration (gastric tumors after oral administration, bladder tumors after intravesical administration, skin tumors after skin application); there are also systemic effects, particularly a high incidence of neurogenic tumors in rodents and dogs and mammary tumors in rodents. MNU is a transplacental carcinogen in rats.

6. Mutagenic and teratogenic effects: MNU is mutagenic in plants and in mice, particularly on protein-free diets. Teratogenic effects have been found in rats.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.

2. Ingestion: Vomiting might reexpose the mouth and esophagus. Drink milk; it may react with nitrosamides. Refer for gastric lavage.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician.

References

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Mirvish, S.S. 1971. Kinetics of nitrosamide formation from alkylureas, N-alkylurethans, and alkylguanidines: Possible implications for the etiology of human gastric cancer. J Natl Cancer Inst 46:1183-1193.

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